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Profile

Biopolis: Village on a Hill

Since the opening of Biopolis in 2003, Singapore's 18 acre science complex on a hill has attracted the rest of the world's curiosity.

What's going on at Centros, Helios, Nanos, and Genome, to name only four of Biopolis's nine geometrically eye-catching buildings (Figure 1)? They leave the impression of stepping into the future, which is right in sync with a larger plan orchestrated by the industrial engineer Philip Yeo. Yeo, chairman first of the Economic Development Board and later of Singapore's A*STAR science agency, saw the need to stimulate Singapore's economy, which, by 2001, was experiencing its steepest downturn since its independence, with an ambitious Biomedical Sciences Initiative.

If all goes according to plan, between 2000 and 2010, the government will have spent roughly 3.5 billion Singaporean dollars on this initiative, and Biopolis will be but one piece of a 200 hectare biomedical development called "One North."

Stem cell science has always been a major part of this initiative, said Lee Eng Hin, a professor of orthopedic surgery at the National University of Singapore and cochairman of the Singapore Stem Cell Consortium (SSCC). Singapore's affinity with stem cells, after all, "goes way back in time," Lee observed. In 1993, Ariff Bongso, a Sri Lankan-born fertility specialist working at the university's hospital, had a vision that the magazine *Asiaweek* described as "a whisper from God" when he grasped the potential medical usefulness of cells from IVF embryos. He went on to isolate them, although he was unable to sustain their growth in vitro beyond two passages.

Biopolis, a broad and busy spectrum of largely government-funded stem cell research—everything from ES to adult cells, basic to clinical—is clear indication of a small nation eager to stay at the forefront. Biopolis houses seven research institutes managed by A*STAR, the Agency for Science, Technology and Research, five of which are heavily involved in stem cells: the Genome Institute of Singapore (GIS), the BioInformatics Institute (BII), the Institute of Molecular and Cell Biology (IMCB), the Bioprocessing Technology Institute (BTI), and the Institute of Medical Biology (IMB). Researchers at the Institute of Bioengineering & Nanotechnology (IBN) also handle stem cells, but to a lesser degree. So far, the only company of the two dozen or so firms located at Biopolis to focus on stem cells is ES Cell International (ESI).

"Biopolis constitutes a fantastic research environment," said ESI's former chief executive Alan Colman. As of July 1, Colman, who is known internationally for helping the Roslin Institute to clone Dolly, moved from Helios to the Proteos building at Biopolis to become the executive director of the Singapore Stem Cell Consortium. "One of the attractive aspects of Biopolis is that it's the way a small island can artificially create critical mass," he noted. "It takes the view that there's no way it can sustain the number and quality of scientists that you'll find in a Boston, or certain other hot areas in North America. But what you can do is bring everyone together as close as possible so that you can maximize the benefit of your resources."

And vast resources Biopolis does have, particularly in the form of people and funding. There are the many distinguished senior scientists from the stem cell and related fields that Philip Yeo lured from other continents, earning him the moniker of "serial kidnapper." There is also local talent, like stem cell researcher Huck-Hui Ng, who might have emigrated had Biopolis not been built. The hope is to boost the local pool to 1000 PhDs by 2015 by way of a national science scholarships program that began in 2001.

Kidnapped husband-wife teams include David Lane, of p53-gene fame, who directs the IMCB institute and is the new chair of the Biomedical Research Council, and Birgitte Lane, who coordinates the study of epithelial stem cells at IMB; UCSD scientists Edward Holmes and Judith Swain were recruited to guide Biopolis's translational medical research; and Neal Copeland and Nancy Jenkins from the National Cancer Institute. Another NCI scientist enticed to Biopolis, Edison Liu, who oversees GIS, in turn recruited hematologist Bing Lim from Harvard Medical School.

Alan Colman came to stay in 2002, when he joined ES Cell International's Singapore office as its first full-time employee. The company, which focuses entirely on human embryonic stem cells, moved to Biopolis a year later. ESI at the time was based in Australia, even though it was a Singapore-registered company. Colman recognized that Singapore, not Australia, presented a brighter future in terms of financing. In Singapore, the attitude toward startups was different, he said. "Yes, there was a desire to make money, but Singapore's decision makers also wanted to increase the sophistication of the work force and bring in people who could mentor the local talent," he recounted. "This double-objective meant there was going to be more of a secure source of financing, at least in the short term, than in Australia."

ESI moved entirely to Biopolis in 2004. The majority of its financing has come from the Singapore government, directly or indirectly, according to Colman, who remains on the company's board. "We would have been dead in the water in the US or UK, because for a private stem cell company, it's very tough to raise money," he said. It's hard for a stem cell company to be profitable within the time frame that investors would like to see a return. This is one reason, he said, that ESI is downsizing its R&D in cell therapies for heart disease and diabetes and upsizing "more near-market opportunities," like making and selling cardiac cells for drug toxicity studies.

Funds available for Biopolis researchers flow from primarily two

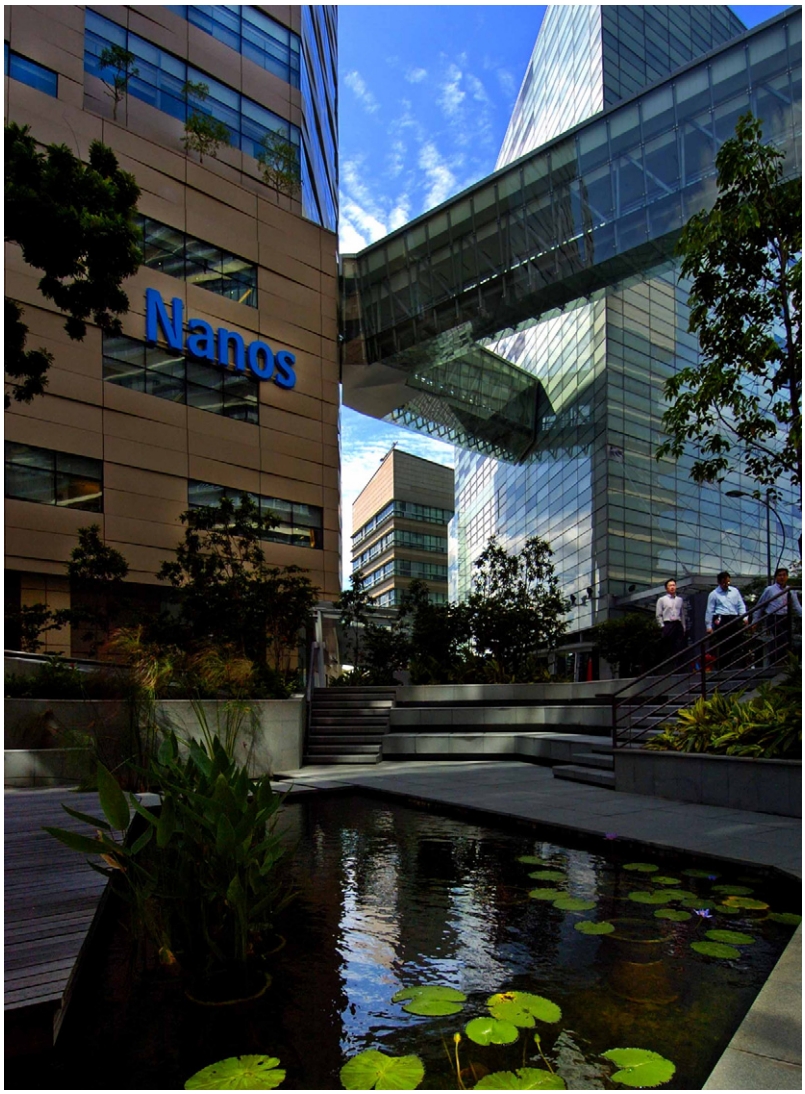

Figure 1. Singapore's Biopolis
Image courtesy of A*STAR, the Agency for Science, Technology and Research.

sources. Each research institute has its own budget, its employees essentially paid by A*STAR. A researcher can also receive funds from the Singapore Stem Cell Consortium, which came into existence in 2005 expressly to coordinate Singapore's stem cell community and nourish it with grant funds. Its support is also government based, because SSCC is under the auspices of the Biomedical Research Council. Last year, SSCC gave out about $10 million in grants, according to Lee.

Bing Lim, the Senior Group Leader for the Genome Institute's Stem Cell and Development Biology Group, appreciates the speed of his institute's intramural funding system. "If something is hot, we can make our own internal decisions and fund it straight away," he described. After a grant proposal is submitted, a meeting of the review committee can be convened in a few days, and, if approved, funding can start almost immediately, he said, whereas "at the NIH, it can take 6–8 months after submitting a grant proposal before you get any funds, if you are successful."

There's a lot about Biopolis's physical location that can encourage collaborations. It has its own academic and corporate epicenter, it is located a few minutes from researchers at the National University and Hospital, and it's smack in the center of one of Asia's most active hubs. "I think the environment is very open for collaborations," said Ian McNiece, who recently joined the Stem Cell Institute at the University of Miami. During the two years he ran Johns Hopkins' research division at Biopolis, "People were very eager to discuss collaborative projects, and we were in the midst of setting some exciting ones up, which added to the disappointment of having to leave." A*STAR terminated its relationship with the Hopkins' Singapore division in the summer of 2006, having spent more than $50 million on the venture. It alleged that Hopkins hadn't accomplished certain milestone markers.

Others have remarked that Biopolis's collaborations between academics and industry could be stronger and that the A*STAR institutes act more like corporate silos than the educational entities they strive to be. Because the stem cell work taking place at Biopolis is raw R&D, with no products yet being manufactured, to what extent the A*STAR institutes can perpetuate entrepreneurial ties, whether with groups close by or far away, remains to be seen.

"It's never easy in any environment to develop working relationships either with other companies or other academics," Colman noted. "There are sensitivities about data, privacy, intellectual property—in any relationship, in any country—and Singapore is no different. Here, because of everyone being close together, it's easier to conceive of and plan for collaborations. But actually getting it all formalized can take longer than you want."

Controls on human embryonic stem cell use are similar to those in the United Kingdom, with stipulations like the 14 day cutoff and no reproductive cloning. There's this difference, however, said Colman: In Singapore, the controls aren't legislated; they are guidelines. "But Singapore has a reputation for authoritarianism, and guidelines have the impact of laws," he said.

The view from outside, that Singapore's regulations are lenient, "is a misconception in my opinion," says Ian McNiece. In his experience, "a lot of uses of human cells were overregulated compared to regulations in the

US,'' he said, and gave this example. ''To purchase existing human cell lines from ATTC for laboratory studies, you needed formal IRB approval, which isn't done in the States. It wasn't hard to get, but it was time consuming, costly, and bureaucratic.''

To move beyond basic research, Biopolis researchers are girding up the staff and infrastructure for translational research. The SSCC, for instance, has given the Bioprocessing Technology Institute the task of building a GMP-grade facility for the expansion of cells for therapies. ''We're aiming for the facility to be functional by mid 2008,'' said Andre Choo, BTI Senior Scientist in human ES cells.

Bing Lim, who began coming over on a part-time basis in 2002 due to Ed Liu's invitation to help launch GIS's stem cell program, now spends most of his time at Biopolis. He feels at home in Singapore, having been born in neighboring Malaysia, plus there are many things about Biopolis that he really likes—the mesh of biology and technology, the highly motivated students he is training, and the collaborative spirit.

At Harvard Medical School, ''You are one person out of hundreds in an academic center that has achieved its pinnacle,'' he remarked. ''You feel you wouldn't be missed. In Singapore, you see a country that is striving to build a center of excellence and constantly raising its own bar, and you know your contribution can matter.''

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